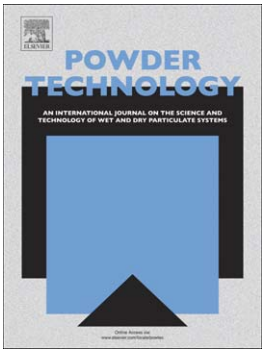


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# Nanonization of ciprofloxacin using subcritical water-ethanol mixture as the solvent: solubility and precipitation parameters

Yuan Pu[a,b], Jundian Lu[a,b], Dan Wang[a,b,*], Fuhong Cai[c], Jie-Xin Wang[a,b], Neil R. Foster[a,d], Jian-Feng Chen[a,b]

[a] *Beijing Advanced Innovation Center for Soft Matter Science and Engineering, State Key Laboratory of Organic-Inorganic Composites, Beijing University of Chemical Technology, Beijing 100029, China*
[b] *Research Center of the Ministry of Education for High Gravity Engineering and Technology, Beijing University of Chemical Technology, Beijing 100029, China*
[c] *College of Mechanical & Electrical Engineering, Hainan University, Haikou 570228, China*
[d] *Department of Chemical Engineering, Curtin University, Perth, Western Australia 6102, Australia*

* Corresponding author: wangdan@mail.buct.edu.cn (D. Wang)

## 1. Introduction

Ciprofloxacin (CIP), a representative member of the quinolones, has been widely used to treat different types of bacterial infections, such as diverse gram-negative infections, urinary tract infections, typhoid fever, pyelonephritis, gonococcal infections, acute sinusitis, just to name a few.[1,2] In nearly all cases, the CIP drug must be dispersed well in solution to be absorbed into the bloodstream from the gastrointestinal tract.[3,4] However, poor aqueous solubility of CIP has been an industry wide problem for its development and clinical application. Recent developments in nanotechnology allows the manipulation of materials at the nanoscale, providing varieties of nanomaterials for diagnosis and therapy.[5-9] Along with others, we have demonstrated that particle size reduction to nanometer can lead to an increased rate of dissolution and higher oral bioavailability [10-14]. Therefore, it is critical to develop CIP nanoparticles with high dissolution rate for oral applications. Solvent anti-solvent precipitation is the most straightforward technique for producing nanoparticles, in which the water insoluble drug is usually dissolved in an organic solvent.[15] However, most drugs produced by precipitation techniques employing organic solvents show trace amounts of solvents even after purification.[16]

Subcritical water (SBCW), also known as superheated water (SHW), hot compressed water (HCW), pressurized hot water (PHW), or near-critical water (NCW), refers to liquid water at temperatures between the atmospheric boiling point of 100 ℃ and the critical temperature of 374 ℃,